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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,255	09/28/2004	Paul Allen Sutton	PC/4-32405A	6345

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
LAO, MARIALOUISA	

ART UNIT	PAPER NUMBER
1621	

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01/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,255	SUTTON ET AL.	
	Examiner	Art Unit	
	M. Louisa Lao	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed 11/13/07 have been fully considered, as follows:

a. the rejection of claims 23-24 under 35 U.S.C. 112, first paragraph, by way of amendment of claim 23 and cancellation of claim 24, is withdrawn. Further, by oversight, claim 22 was intended to be rejected with claims 23-24, since claim 22 recites the pharmaceutical composition of claims 23-24, and is not a new rejection.

b. the rejection of claim 7 under 35 U.S.C. 112, second paragraph is withdrawn.

c. the rejection of claims 1-23 under 35 U.S.C. 103(a), but they are not persuasive. See discussion below.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 22 is rejected under 35 U.S.C. 112, first paragraph – scope of enablement, because the specification, while being enabling for a pharmaceutical composition for the treatment of diabetes, does not reasonably provide enablement for a pharmaceutical composition for the treatment of cardiovascular diseases or conditions associated therewith. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. ***A disclosed species can not support a generic claim.*** The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount

of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in the art, g) the predictability or unpredictability of the art, and, h) the breadth of the claims.

3. In the present case, the important factors leading to a conclusion of undue experimentation are the absence of any working example of a pharmaceutical composition for the treatment of cardiovascular diseases or conditions associated therewith, the lack of predictability in the art, the amount of direction and guidance provided and the broad scope of the claim.

a) the amount of experimentation needed. There is a plurality of cardiovascular diseases or conditions associated therewith. In the same light a pharmaceutical composition for the variety of methods of treatment, dose, form of administration, the quantity of experiments and corresponding clinical trials thereto, would likewise be numerous.

b) the amount of direction and guidance provided. The specification on page 18-22 recites the *in vivo* tests in mice for blood glucose control and illustrates *in vivo* test for HbA_{1c}.

c) the presence or absence of working examples. There are no working examples of a pharmaceutical composition for the method for the treatment of cardiovascular diseases or conditions associated therewith.

d) the nature of the invention and the e) the state of the prior art. Compounds of the nateglinide, free-form and as pharmaceutically acceptable salt form as recited in the instant claims are known, see Guitard et al. (US694955, US`555).

f) the relative skill of those in the art. The skilled artisans are synthetic organic chemists and clinical pharmacists with graduate degrees and potentially with many years of research and industrial experience.

g) the predictability or unpredictability of the art. The state of the art of method of treatment is unpredictable, since this art is largely empirical, which requires fulfilling a rationale for the optimization of absorption, distribution, metabolism, and excretion of a drug. Determining whether a compound meets the attributes of a useful prodrug entails substantial clinical testing with laborious experimentation. See cited reference in Office Action dated 5/11/07, Goodman & Gilman's *The Pharmacological Basis of Therapeutics".* 10th ed. NY McGraw Hill 2001 p3.

h) the breadth of the claim. Claim 22 recites a pharmaceutical composition for the treatment of cardiovascular diseases or conditions associated therewith. This is broad. Further, it is unclear whether the applicants intend to encompass *all conditions* associated with cardiovascular diseases. The recitation of disorders like, *inter alia,* cataracts, erectile dysfunction, premenstrual syndrome, skin and connective tissue disorders, osteoporosis, polycystic ovary syndrome, stroke are conditions that *may* not necessarily ensue from cardiovascular diseases.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed.Cir.1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Thus, the scope of enablement of the instant specification is not commensurate to the invention as recited.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guitard et al. (US6949555, US`555).

8. The instant claims are drawn to a salt of nateglinide, with physical attributes, relative to melting point and solubility; and chemical attributes, relative to cation to anion ratios, thereto as recited therein.

9. US`555 teaches the use of organic compounds, where said compounds are hypolipidemic agents or pharmaceutically acceptable salts thereof for the manufacture of a medicament for, *inter alia,* diabetes, microvascular complications, cardiovascular mortality. In column 9 lines 30-52, US`555 states that the said compounds like, *inter alia,* nateglinide, repaglinide, metformin, may be used for separate use or as a fixed combination. In lines 5-16 column 10,

US`555 teaches that said compounds to be combined can be present as pharmaceutically acceptable salts including, *inter alia,* acid addition salts and exemplified therein is *nateglinide forming pharmaceutically acceptable salts with bases, namely cationic salts, such as alkali and alkaline earth metal salts, as well as ammonium salts.* In column 10 lines 49-54, US`555 describes the doses for use of said compound are those that are being used for agents that have already been launched. In column 12 US`555 teaches the method as for example in lines 52-55, *inter alia,* for treating conditions and diseases associated with IGM (Impaired Glucose Metabolism) or IFG (Impaired Fasting Glucose) comprising administering a nateglinide agent or a pharmaceutically acceptable salt thereof to subjects in need thereof.

10. Albeit, US`555 is silent on explicitly describing the physical and chemical attributes of the pharmaceutically acceptable salts of said compounds (like nateglinide), including the ratio of cation to anion to make said salt compositions, the Examiner takes the stand that the salts of US`555 are the same as the instant application's, absent a comparative showing to attest thereto of the difference.

11. At the time of the invention, one of ordinary skill in the art looking for acceptable forms of nateglinide would have found it obvious to utilize the teachings of US`555 in making the salts of nateglinide. US`555 has shown that the pharmaceutically acceptable salts of nateglinide can be made.

12. One having ordinary skill in the art would have been motivated to make the salts of nateglinide, and reached a reasonable expectation of success; since US`555 has shown that the free or salt forms are efficacious singly as active agents or in combination with other organic hypolipidemic agents.

13. The teachings of the cited prior art are fairly suggestive of the *prima facie* obviousness of the instant claims, as recited.

- Applicants argue that the instant salts have unique and desirable chemical and/or physical characteristics that are not disclosed or suggested by US`555, which include *inter alia* higher degree of dissociation in water, increased biological activity, exceptional physical stability, retention of melting point.
- However, said salts have been taught by the cited art reference, US`555 as discussed in the Office Action mailed 5/11/07. To reiterate, the instant salts are unpatentable, the expectation of success of one of ordinary skill in the art at the time of Applicants' invention in making other salts need only be reasonable, and not because the formation and properties of each salt must be verified through testing. Merck, 874F.2d at 809; In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1998) *cited in* Pfizer Inc. v. Apotex, Inc. March2007.
- Further, in light of the Pfizer Inc. v. Apotex, Inc. March2007 findings, the salts of an existing compound (nateglinide) are obvious.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MLouisa Lao whose telephone number is 571-272-9930. The examiner can normally be reached on Mondays to Thursdays from 8:00am to 8:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Karl Puttlitz/
Art Unit 1621

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TC1600 GAU 1621